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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,835	01/30/2002	Thomas Richardson	UMICH-11	2416

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EXAMINER	
BETTON, TIMOTHY E	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/058,835	RICHARDSON ET AL.	
	Examiner	Art Unit	
	Timothy E. Betton	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33--36,38,40,42 and 44-60* is/are pending in the application.

4a) Of the above claim(s) *,34,44, 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *33,35,36,38,40,42 and 46-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election with traverse in the reply filed on 15 June 2006 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant invention.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

Claims 33, 35, 36, 38, 40, 42, 44-60 are pending for prosecution on the merits. Claims 51-60 are new.

Election

Applicants elect Group III, drawn to methods for eliminating or reducing normal but undesired adipose tissue in a patient by administering a small molecule drug, such as a beta-adrenergic stimulator substance.

Claim Rejections-35 USC 112, 1ST Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claims 33 and 47 disclose the terms "eliminate " and/or "prevent". The specification contains no adequate written description of the exact preventive properties of claimed invention. Further, there is no adequate disclosure of a proper manner and/or process of making or using the claimed invention. The central issue of the claimed invention is a method for eliminating or reducing normal but undesired adipose tissue, of which the said formulation comprising a substance, which "eliminates" or "prevents" formation of the cells of adipose tissue. The specification fails to disclose a clear, concise, and exact description as to enable any person skilled in the art to make and/or use claimed invention.

Claim Rejections-35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 33 is maintained as rejected under 35 U.S.C. 102(b) as being anticipated by Goldenberg et al.

Applicant asserts that Goldenberg et al. do not anticipate the invention because they do not disclose a method where the sustained release formulation is administered by "injection at a local area containing the undesired tissue".

Goldenberg et al. disclose that mice were injected subcutaneously in the neck. As Applicants argued in the traversal of the 112, second paragraph rejection, the term "local area" as defined in the International Dictionary of Medicine and Biology includes a region of the body. With injection into the neck, the trunk of the mouse would be a "local area". Since fat tissue is distributed throughout the body, this injection would necessarily involve injection into a local area containing the undesired tissue. Applicant further argues that the reference of Goldenberg et al. discusses overall weight loss, not loss of undesired tissue in the local area of the injection. However, it is well-known in the art that weight loss is associated with reduction of fat tissue. An overall weight loss would include reduction of fat tissue in the trunk and hence the local area as defined by Applicant.

Claim Rejections- 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg et al. under 35 USC 102(b) for the reasons of record set forth in the Office Action mailed August 12, 2004.

Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg et al. in view of Hutchinson et al., Ogawa et al. or Johnson et al. for the reasons of record set forth in the Office Action mailed August 12, 2004.

Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg et al., and further in view of Silvestri et al. for the reasons of record set forth in the Office Action mailed August 12, 2004.

Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg et al. and Silvestri et al. as applied to claims 33 above, and further in view of Merwin et al. for the reasons of record set forth in the Office Action mailed August 12, 2004.

In traversing each of the 103 rejections, Applicant argues that Goldenberg et al. do not teach injection of a controlled release formulation at a local area containing the undesired tissue and do not suggest use of a sustained-release formulation for the purposes of reducing tissue in a local area. For each 103 rejection Applicant argues that the other cited references do not make up for the deficiencies of the Goldenberg et al. reference and thus all 103 rejections should be withdrawn. These arguments have been fully considered but are not persuasive because Goldenberg et al. do teach injection of a sustained release formula at a local area containing the undesired tissue. Goldenberg et al. teach subcutaneous injection in the neck, which makes the trunk of the animal a "local area" as per Applicant's definition of this term. Goldenberg et al. teach overall

weight loss which would include reduction of fat tissue in a local area as defined by Applicant.

Claims 35,36, 38, and 51-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richardson et al. (PG PUB US 2003/0022856 A1) in view of Greenway, III et al. (USPN 4,525,359) and Greenway III, et al. (USPN 4,588,724).

Richardson et al. teach methods for ablation, i.e., elimination or reduction, of unwanted tissue, particularly tissue which is normal to be present in the body but is unwanted for either health or cosmetic reasons. In particular embodiments, there are described methods for elimination of fat tissue from the body. According to the methods described herein, a drug which acts to eliminate the undesired tissue is provided in a carrier which is biocompatible, capable of being administered by injection, and which effects a controlled release of the drug over time. The drug with carrier is administered by injection locally in the area of the unwanted tissue, resulting in elimination of the tissue in that local area. Richardson et al teach administration beta-adrenergic stimulators [0006], sustained-release dosage form of invention [0007], poly(lactide-co-glycolide) material [0014], and microspheres [0023, 0032] with the exact weight range taught [0016].

Greenway, III et al. (USPN 4,525,359) and (USPN 4,588,724) both teach a treatment for accelerating regional weight reduction in humans, wherein an active ingredient encouraging elimination of fatty deposits, preferably a beta adrenergic stimulator or an alpha-2 adrenergic inhibitor, is selectively delivered to a regional fat deposit prior to commencing or during a general weight control program, whereby body

weight is preferentially reduced in the selected area. The beta adrenergic stimulator preferably isoproterenol or forskolin, or the alpha-2 adrenergic inhibitor, preferably yohimbine, or combinations thereof may be delivered by any means accomplishing specific delivery to the selected area, including injection, implantation, and topical application to the skin as in an ointment or crème (Abstract).

Richardson et al, and Greenway, III et al ('359, '724) do not specifically teach cytokine regulatory activity. However, Girten et al. teaches novel peptides that are potent cytokine regulatory agents. In addition, the present invention relates to pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a cytokine regulatory agent. Administration of such a cytokine regulatory agent to a subject can enhance or restrain cytokine activity. Thus, the present invention provides a method of regulating cytokine activity in a subject having a condition characterized by aberrant or altered cytokine activity. The invention also provides methods of treating such conditions, including, for example, disuse deconditioning, diseases mediated by nitric oxide and cytokines, adverse drug reactions, obesity, septic shock, and adverse side effects due to cancer chemotherapy or occurring as in response to organ transplantation (Abstract)

Thus, it would be prima facie obvious to combine the methods of Richardson et al. with the methods of Greenway, III et al. One of ordinary skill in the pertinent art would at once see the reasonable expectation of success via the incorporating together of Richardson et al. and Greenway, III et al. Instant claim 33 discloses a method for eliminating or reducing normal but undesired adipose tissue in a patient which

comprises administering a controlled release formulation to the patient by injection into the adipose tissue at a local area such that undesired adipose tissue in the local area is selectively eliminated or reduced, said formulation comprising a substance which eliminates or prevents formation of the Cells of adipose tissue, said substance being provided in a controlled release carrier. Richardson et al. and Greenway, III et al. both are obvious over claimed invention because of their encompassing every element of the claimed subject matter of claimed invention. Additionally, Girten et al. is the motivation to further combine due to said patented reference teaching general methods of cytokine regulatory agents.

Response to Arguments

Applicants' remarks filed 15 June 2006 have been acknowledged. The traversal is on the ground(s) that the requirement for restriction was not properly made. This is not found persuasive because applicants fail to disclose a factual basis upon their alleged claims.

The instant invention is drawn toward a practicing method for eliminating or reducing normal but undesired adipose tissue in a patient which comprises administering a controlled release formulation to the patient by injection into the adipose tissue at a local area such that undesired adipose tissue in the local area is selectively eliminated or reduced, said formulation comprising a substance which eliminates or prevents formation or reduces the lipid content of the cells of adipose tissue, said substance being provided in a controlled release carrier.

Applicants have elected Group III: Claims 35, 36, 38, 40, 42 and 46-50, drawn to a method of eliminating or reducing adipose tissue in a patient by administration of a substance that is a drug that kills fat cells including those that are cytokine regulatory agents, beta-adrenergic stimulators or alpha-2 adrenergic inhibitors, classifiable in class 514, subclass 1. The two-way distinctiveness is met. The inventions as claimed can have a materially different design, mode of operation, function, or effect. In the instant case, the inventions are directed to use of different products. The inventions are distinct, each from the other because of the following reasons:

Inventions I-III are directed to related processes. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j)

The invention of claim I uses a substance that is a protein to eliminate or reduce adipose tissue, invention II uses a substance that is a nucleic acid to eliminate or reduce adipose tissue and invention III uses a substance that is a small molecule to eliminate or reduce adipose tissue. Therefore, the inventions do not overlap in scope, are not obvious variants and have different design.

Claim 33 is rejected over prior art as disclosed above. The restriction requirement is thus supported and maintained.

An entire scope of an invention can be burdensome if all elements are examined together. Furthermore, examining any of inventions I-III together would impose a

serious search burden. In the instant case, prior art searches of methods of using proteins to eliminate or reduce adipose tissue are not coextensive with prior art searches of methods of using nucleic acids or small molecules to eliminate or reduce adipose tissue. Search of each of these inventions would require different key word searches of each compound and of each distinctive step of the method using divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious burden on the Office in terms of search and examination.

Claim 33 link(s) inventions I-III. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 33. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312. Applicant(s) are advised that if any claim(s) including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

In regard to the previous prior art rejections, applicants respectfully urge that the cited prior art does not anticipate or render obvious the claimed invention. Applicants' arguments have been fully considered but they are not persuasive. Goldenberg adequately discloses a method wherein the controlled release formulation is injected "into the adipose tissue" Goldenberg et al. disclose that mice were injected subcutaneously in the neck. As Applicants argued in the traversal of the 112, second paragraph rejection, the term "local area" as defined in the International Dictionary of Medicine and Biology includes a region of the body. With injection into the neck, the trunk of the mouse would be a "local area". Since fat tissue is distributed throughout the body, this injection would necessarily involve injection into a local area containing the undesired tissue. Applicant further argues that the reference of Goldenberg et al. discusses overall weight loss, not loss of undesired tissue in the local area of the injection. However, it is well-known in the art that weight loss is associated with reduction of fat tissue. An overall weight loss would include reduction of fat tissue in the trunk and hence the local area as defined by Applicant.

Further, applicants' traverse the Hutchinson, Ogawa, Merwin, or Johnson articles and Silvestri (USPN 5,126,147), that there is no suggestion in any of references that a specific local area of adipose tissue could be targeted. However, one of ordinary skill in the pertinent art would at once recognize the necessity of the administration of

said agents to key, predetermined regions of the human epidermis that will produce the greatest therapeutic response.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

Ardin H Marschel 11/2/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER